



STIC Search Report

Biotech-Chem Library

STIC Database Tracking Number: 98051

TO: Laurie A Mayes
Location: r 10A16; m 9B01
Art Unit: 1653
Thursday, July 03, 2003

Case Serial Number: 09/819098

From: Barb O'Bryen
Location: Biotech-Chem Library
CM1-6A05
Phone: 308-4291 *BOB*

barbara.obryen@uspto.gov

Search Notes

Ex. Mayes,
there isn't a way to force a non-specific mutation at a particular point in a sequence for doing a search. (i.e. we don't have way, in our standard search system, to say, "position 309 is any amino acid *other than* Phe"). I retrieved the sequence you specified from the NCBI website & searched it. If matches are found to seqs with mutations at 309 or 562, the mutations will show up as non-matches or conservative substitutions at those points.

Please let me know if you have any questions.

Barb O'Bryen

308-4291

JOURNAL Biochemistry 41 (37), 11269-11276 (2002)
MEDLINE [22209045](#)
PUBMED [12220193](#)
REMARK GeneRIF: The activation of procofactor VIII to factor VIIIA increases the affinity of binding to platelets of both factor VIIIA and factor X.

REFERENCE 5 (residues 1 to 2351)
AUTHORS Bogdanova,N., Markoff,A., Pollmann,H., Nowak-Gottl,U., Eisert,R., Dworniczak,B., Eigel,A. and Horst,J.
TITLE Prevalence of small rearrangements in the factor VIII gene F8C among patients with severe hemophilia A
JOURNAL Hum. Mutat. 20 (3), 236-237 (2002)
MEDLINE [22191118](#)
PUBMED [12204009](#)
REMARK GeneRIF: Reported nine novel (6 deletions, two indels and one partial duplication) and five recurrent small rearrangements identified in 15 German patients with severe hemophilia A.

REFERENCE 6 (residues 1 to 2351)
AUTHORS Frusconi,S., Passerini,I., Girolami,F., Masieri,M., Linari,S., Longo,G., Morfini,M. and Torricelli,F.
TITLE Identification of seven novel mutations of F8C by DHPLC
JOURNAL Hum. Mutat. 20 (3), 231-232 (2002)
MEDLINE [22191107](#)
PUBMED [12203998](#)
REMARK GeneRIF: Seven novel mutations causing severe, moderate and mild Hemophilia A.

REFERENCE 7 (residues 1 to 2351)
AUTHORS Jenkins,P.V., Freas,J., Schmidt,K.M., Zhou,Q. and Fay,P.J.
TITLE Mutations associated with hemophilia A in the 558-565 loop of the factor VIIIA A2 subunit alter the catalytic activity of the factor Xase complex
JOURNAL Blood 100 (2), 501-508 (2002)
MEDLINE [22085818](#)
PUBMED [12091341](#)
REMARK GeneRIF: Mutations associated with hemophilia A in the 558-565 loop of the factor VIIIA A2 subunit alter the catalytic activity of the factor Xase complex.

REFERENCE 8 (residues 1 to 2351)
AUTHORS Ananyeva,N.M., Kouivavskaja,D.V., Shima,M. and Saenko,E.L.
TITLE Intrinsic pathway of blood coagulation contributes to thrombogenicity of atherosclerotic plaque
JOURNAL Blood 99 (12), 4475-4485 (2002)
MEDLINE [22032682](#)
PUBMED [12036878](#)
REMARK GeneRIF: increased procoagulant activity due to formation of additional fVIII phosphatidylserine binding sites on the outer surface of oxLDL-treated cells and higher binding affinity between components of the Xase complex, activated factors VIII and IX.

REFERENCE 9 (residues 1 to 2351)
AUTHORS Koszelak Rosenblum,M.E., Schmidt,K., Freas,J., Mastri,M. and Fay,P.J.
TITLE Cofactor activities of factor VIIIA and A2 subunit following cleavage of A1 subunit at Arg336
JOURNAL J. Biol. Chem. 277 (14), 11664-11669 (2002)
MEDLINE [21922803](#)
PUBMED [11799130](#)
REMARK GeneRIF: Cofactor activities of factor VIIIA and A2 subunit following cleavage of A1 subunit at Arg336

REFERENCE 10 (residues 1 to 2351)
AUTHORS Obratsov,I.F., Kuz'min,V.M., Khanin,M.A., Kogan,A.E.,

Anan'eva,N.M. and Saenko,E.L.
 TITLE Effect of factor VIII deficiency on generation of thrombin: a biomechanical approach
 JOURNAL Dokl Biochem Biophys 383, 119-121 (2002)
 MEDLINE [22054191](#)
 PUBMED [12058364](#)
 REMARK GeneRIF: Effect of deficiency on generation of thrombin
 REFERENCE 11 (residues 1 to 2351)
 AUTHORS Cutler,J.A., Mitchell,M.J., Smith,M.P. and Savidge,G.F.
 TITLE The identification and classification of 41 novel mutations in the factor VIII gene (F8C)
 JOURNAL Hum. Mutat. 19 (3), 274-278 (2002)
 MEDLINE [21846190](#)
 PUBMED [11857744](#)
 REMARK GeneRIF: Forty-one novel causative factor VIII gene mutations have been identified and classified in hemophiliacs.
 REFERENCE 12 (residues 1 to 2351)
 AUTHORS Liu,M.L., Nakaya,S. and Thompson,A.R.
 TITLE Non-inversion factor VIII mutations in 80 hemophilia A families including 24 with alloimmune responses
 JOURNAL Thromb. Haemost. 87 (2), 273-276 (2002)
 MEDLINE [21847284](#)
 PUBMED [11858487](#)
 REMARK GeneRIF: Heteroduplex screening identified 74 small mutations in the F8 genes of 72 families with hemophilia A. In 24 families, at least one affected member had an alloimmune response to F8: of these, 11 were associated with missense mutations.
 REFERENCE 13 (residues 1 to 2351)
 AUTHORS Stoilova-McPhie,S., Villoutreix,B.O., Mertens,K., Kemball-Cook,G. and Holzenburg,A.
 TITLE 3-Dimensional structure of membrane-bound coagulation factor VIII: modeling of the factor VIII heterodimer within a 3-dimensional density map derived by electron crystallography
 JOURNAL Blood 99 (4), 1215-1223 (2002)
 MEDLINE [21818513](#)
 PUBMED [11830468](#)
 REMARK GeneRIF: 3-Dimensional structure of membrane-bound coagulation factor VIII from electron crystallography
 REFERENCE 14 (residues 1 to 2351)
 AUTHORS Khrenov,A., Sarafanov,A., Ananyeva,N., Kouliavskaia,D., Shima,M., Schwinn,H., Josic,D. and Saenko,E.
 TITLE Molecular basis for different ability of low-density and high-density lipoproteins to support activity of the intrinsic Xase complex
 JOURNAL Thromb. Res. 105 (1), 87-93 (2002)
 MEDLINE [21854514](#)
 PUBMED [11864712](#)
 REMARK GeneRIF: Activation by thrombin dramatically increased fVIII affinity for LDL but not HDL, which may be related to differences in phospholipid composition of the LPs.
 REFERENCE 15 (residues 1 to 2351)
 AUTHORS Xie,Y.G., Zheng,H., Leggo,J., Scully,M.F. and Lillicrap,D.
 TITLE A founder factor VIII mutation, valine 2016 to alanine, in a population with an extraordinarily high prevalence of mild hemophilia A
 JOURNAL Thromb. Haemost. 87 (1), 178-179 (2002)
 MEDLINE [21836995](#)
 PUBMED [11848452](#)
 REMARK GeneRIF: A founder factor VIII mutation, valine 2016 to alanine, was found in a Newfoundland population with an extraordinarily high

- prevalence of mild hemophilia A.
- REFERENCE 16 (residues 1 to 2351)
- AUTHORS Brummer,J., Groth,J., Flayeh,R., Wagener,C. and Jung,R.
- TITLE Absence of mutations at the APC interacting sites of factor VIII in Caucasians
- JOURNAL Thromb. Haemost. 87 (1), 170 (2002)
- MEDLINE [21836989](#)
- PUBMED [11848448](#)
- REMARK GeneRIF: No mutations at the APC interacting sites exons 8, 11, & 19) of factor VIII were found in Caucasians with recurrent deep venous thrombosis.
- REFERENCE 17 (residues 1 to 2351)
- AUTHORS Reipert,B.M., Sasgary,M., Ahmad,R.U., Auer,W., Turecek,P.L. and Schwarz,H.P.
- TITLE Blockade of CD40/CD40 ligand interactions prevents induction of factor VIII inhibitors in hemophilic mice but does not induce lasting immune tolerance
- JOURNAL Thromb. Haemost. 86 (6), 1345-1352 (2001)
- MEDLINE [21632021](#)
- PUBMED [11776297](#)
- REFERENCE 18 (residues 1 to 2351)
- AUTHORS Bogdanova,N., Lemcke,B., Markoff,A., Pollmann,H., Dworniczak,B., Eigel,A. and Horst,J.
- TITLE Seven novel and four recurrent point mutations in the factor VIII (F8C) gene
- JOURNAL Hum. Mutat. 18 (6), 546 (2001)
- MEDLINE [21614886](#)
- PUBMED [11748850](#)
- REMARK GeneRIF: Eleven pathological changes in the factor VIII sequence detected in male patients with haemophilia A or in female obligate carriers.
- REFERENCE 19 (residues 1 to 2351)
- AUTHORS Long,G., Zhu,C. and Liu,J.
- TITLE The significance of nucleotide repeat sequences in FVIII gene for detecting hemophilia A carriers
- JOURNAL Zhonghua Xue Ye Xue Za Zhi 22 (10), 511-513 (2001)
- MEDLINE [21620598](#)
- PUBMED [11769673](#)
- REMARK GeneRIF: Fourteen of the 21 females were confirmed to be carriers.
- REFERENCE 20 (residues 1 to 2351)
- AUTHORS Maugard,C., Tuffery,S., Aguilar-Martinez,P., Schved,J.F., Gris,J.C., Demaille,J. and Claustres,M.
- TITLE Protein truncation test: detection of severe haemophilia a mutation and analysis of factor VIII transcripts
- JOURNAL Hum. Mutat. 11 (1), 18-22 (1998)
- MEDLINE [98111374](#)
- PUBMED [9450898](#)
- REFERENCE 21 (residues 1 to 2351)
- AUTHORS Bowen,D.J. and Hampton,K.K.
- TITLE Analysis of the BglI restriction fragment length polymorphism in the human factor VIII gene using 'virtual PCR'--a novel approach employing the polymerase chain reaction in the absence of sequence information for the locus
- JOURNAL Hum. Genet. 98 (2), 219-222 (1996)
- MEDLINE [96305455](#)
- PUBMED [8698347](#)
- REFERENCE 22 (residues 1 to 2351)
- AUTHORS Lakich,D., Kazazian,H.H. Jr., Antonarakis,S.E. and Gitschier,J.
- TITLE Inversions disrupting the factor VIII gene are a common cause of severe haemophilia A

JOURNAL Nat. Genet. 5 (3), 236-241 (1993)
 MEDLINE [94100976](#)
 PUBMED [8275087](#)
 REFERENCE 23 (residues 1 to 2351)
 AUTHORS Levinson,B., Kenwrick,S., Gamel,P., Fisher,K. and Gitschier,J.
 TITLE Evidence for a third transcript from the human factor VIII gene
 JOURNAL Genomics 14 (3), 585-589 (1992)
 MEDLINE [93052386](#)
 PUBMED [1427887](#)
 REFERENCE 24 (residues 1 to 2351)
 AUTHORS Gitschier,J. and Wood,W.I.
 TITLE Sequence of the exon-containing regions of the human factor VIII gene
 JOURNAL Hum. Mol. Genet. 1 (3), 199-200 (1992)
 MEDLINE [93265012](#)
 PUBMED [1303178](#)
 REFERENCE 25 (residues 1 to 2351)
 AUTHORS Gitschier,J.
 TITLE The molecular basis of hemophilia A
 JOURNAL Ann. N. Y. Acad. Sci. 614, 89-96 (1991)
 MEDLINE [91221499](#)
 PUBMED [1902642](#)
 REFERENCE 26 (residues 1 to 2351)
 AUTHORS Patterson,M., Gitschier,J., Bloomfield,J., Bell,M., Dorkins,H., Froster-Iskenius,U., Sommer,S., Sobell,J., Schaid,D., Thibodeau,S. et al.
 TITLE An intronic region within the human factor VIII gene is duplicated within Xq28 and is homologous to the polymorphic locus DXS115 (767)
 JOURNAL Am. J. Hum. Genet. 44 (5), 679-685 (1989)
 MEDLINE [89205550](#)
 PUBMED [2565080](#)
 REFERENCE 27 (sites)
 AUTHORS Youssoufian,H., Wong,C., Aronis,S., Platokoukis,H., Kazazian,H.H. Jr. and Antonarakis,S.E.
 TITLE Moderately severe hemophilia A resulting from Glu----Gly substitution in exon 7 of the factor VIII gene
 JOURNAL Am. J. Hum. Genet. 42 (6), 867-871 (1988)
 MEDLINE [88220354](#)
 PUBMED [2835904](#)
 REFERENCE 28 (sites)
 AUTHORS Bernardi,F., Legnani,C., Volinia,S., Patracchini,P., Rodorigo,G., DeRosa,V. and Marchetti,G.
 TITLE A HindIII RFLP and a gene lesion in the coagulation factor VIII gene
 JOURNAL Hum. Genet. 78 (4), 359-362 (1988)
 MEDLINE [88197150](#)
 PUBMED [2896159](#)
 REFERENCE 29 (residues 1 to 2351)
 AUTHORS Truett,M.A., Blacher,R., Burke,R.L., Caput,D., Chu,C., Dina,D., Hartog,K., Kuo,C.H., Masiarz,F.R., Merryweather,J.P. et al.
 TITLE Characterization of the polypeptide composition of human factor VIII:C and the nucleotide sequence and expression of the human kidney cDNA
 JOURNAL DNA 4 (5), 333-349 (1985)
 MEDLINE [86081164](#)
 PUBMED [3935400](#)
 REFERENCE 30 (residues 1 to 2351)
 AUTHORS Gitschier,J., Wood,W.I., Tuddenham,E.G., Shuman,M.A., Goralka,T.M., Chen,E.Y. and Lawn,R.M.
 TITLE Detection and sequence of mutations in the factor VIII gene of

haemophiliacs

JOURNAL Nature 315 (6018), 427-430 (1985)

MEDLINE [85213871](#)

PUBMED [2987704](#)

REFERENCE 31 (residues 1 to 2351)

AUTHORS Toole,J.J., Knopf,J.L., Wozney,J.M., Sultzman,L.A., Buecker,J.L., Pittman,D.D., Kaufman,R.J., Brown,E., Shoemaker,C., Orr,E.C. et al.

TITLE Molecular cloning of a cDNA encoding human antihemophilic factor

JOURNAL Nature 312 (5992), 342-347 (1984)

MEDLINE [85061550](#)

PUBMED [6438528](#)

REFERENCE 32 (residues 1 to 2351)

AUTHORS Wood,W.I., Capon,D.J., Simonsen,C.C., Eaton,D.L., Gitschier,J., Keyt,B., Seeburg,P.H., Smith,D.H., Hollingshead,P., Wion,K.L. et al.

TITLE Expression of active human factor VIII from recombinant DNA clones

JOURNAL Nature 312 (5992), 330-337 (1984)

MEDLINE [85061548](#)

PUBMED [6438526](#)

COMMENT REVIEWED [REFSEQ](#): This record has been curated by NCBI staff. The reference sequence was derived from [M14113.1](#).

Summary: This gene encodes coagulation factor VIII, which participates in the intrinsic pathway of blood coagulation; factor VIII is a cofactor for factor IXa which, in the presence of Ca²⁺ and phospholipids, converts factor X to the activated form Xa. This gene produces two alternatively spliced transcripts. Transcript variant 1 encodes a large glycoprotein, isoform a, which circulates in plasma and associates with von Willebrand factor in a noncovalent complex. This protein undergoes multiple cleavage events. Transcript variant 2 encodes a putative small protein, isoform b, which consists primarily of the phospholipid binding domain of factor VIIIC. This binding domain is essential for coagulant activity. Defects in this gene results in hemophilia A, a common recessive X-linked coagulation disorder.

Transcript Variant: This variant (1) is the full length product and includes 26 exons.

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<u>Protein</u>	1..2351 /product="coagulation factor VIII isoform a precursor" /note="coagulation factor VIIIC; procoagulant component"
<u>sig_peptide</u>	1..19
<u>mat_peptide</u>	20..2351 /product="coagulation factor VIIIC, isoform a"
<u>mat_peptide</u>	20..1332 /product="activated factor VIIIC heavy chain (200 kda)"
<u>mat_peptide</u>	20..759 /product="activated factor VIIIC heavy chain (92 kda)"
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 /note="by thrombin"
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 /note="Cu-oxidase"
 /db_xref="CDD:pfam00394"
Site 759..760
 /site_type="cleavage"
 /note="by thrombin"
mat_peptide 1668..2351
 /product="activated factor VIIIC light chain (80 kda)"
Site 1708..1709
 /site_type="cleavage"
 /note="by thrombin"
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 /note="Cu-oxidase"
 /db_xref="CDD:pfam00394"
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 /note="Isoform a is encoded by variant 1."
 /db_xref="LocusID:2157"
 /db_xref="MIM:306700"

ORIGIN

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121 gvsywkaseg aeyddqtsqr ekeddkvfpg gshtyvwqvl kengpmasdp lcltysylsh
181 vdlvkdlmsg ligallvcre gslakektqt lkhfillfav fdegkswhse tknslmqdrd
241 aasarawpkm htvnqyvnrs lpgligchrk svywhvigmg ttpevhsifl eghtflvrnh
301 rqaasleispi tfltaqtllm dlqgflfch issqhhdgme ayvkvdsce epqlrmkne
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1741 aqsgsvppqfk kvvfqeftdg sftqplyrge lnehlgl1gp yiraevedni mvtfrnqasr
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1981 vftvrkkeey kmalynlypg vftvemlps kagiwrvecl ige1lhagms t1flvysnkc
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2281 isssqdghqw tlffqngkvk vfgqnqdsft pvnsl1dppl ltrylrihpq swvhqialrm
2341 evlgceaql y

//

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Jun 19 2003 12:37:45